

Exhibit 7

cA2 Marketing Plan

U.S. Crohn's Indication Launch

March 25, 1998

Plaintiffs' Exhibit

249

01-12257-PBS

EXHIBIT

Holbeck 3
1213164

PERIOD 800-431-4930

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MDL-CEN00002717

cA2 Marketing Plan

■ Presentation Overview

- Situation Analysis
- Payer Analysis
- Product Overview
- SWOT Analysis
- Key Imperatives
- Key Strategies

cA2 Marketing Plan

■ Key Strategies

- Clinical Positioning Strategy
- Payer Positioning Strategy
- Economic Platform Strategy
- Integrated Services Strategy
 - » Product Access Plan
 - » Admin Supplies Plan
 - » Reimbursement Support Plan
 - » Infusion Services Support
- Contracting Strategy
- Pricing Strategy
- Patient Pull Strategy
- RA Pre Approval Strategy
- Market Expansion Strategy
- cA2 Selling Process

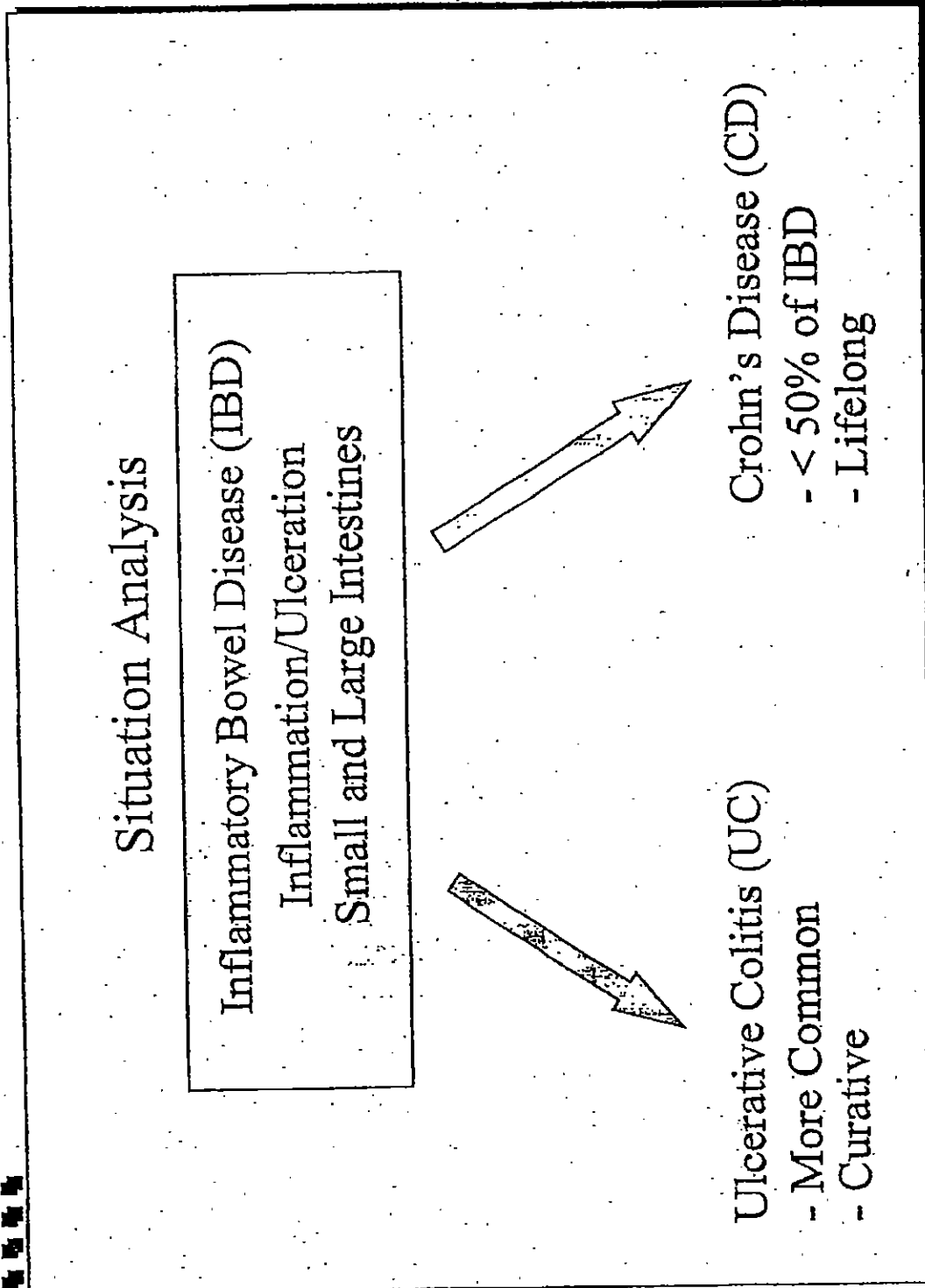
cA2 Marketing Plan Situation Analysis

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Situation Analysis

- Inflammatory Bowel Disease
- Crohn's Disease
 - Incidence/Prevalence
 - Patient
 - Physician
 - Treatment
- Future Developments
- Summary/Conclusions



Situation Analysis Comparative Features in Ulcerative Colitis and Crohn's Disease

	Ulcerative Colitis	Crohn's Disease
Site of Disease	Limited to colon	Anywhere in GI tract
Affliction	Curable	Lifelong
Acute, toxic symptoms	Common in severe disease	Unusual
Stools	Bloody, watery with mucus	Mushy, watery, blood unusual
Perirectal involvement	Occurs in 10-20% but is usually self-limiting	Deep fissures, abscesses, or fistulas in 50%
Sigmoidoscopy	Granular mucosa typical, friable mucosa, small pitting ulcerations	Granular mucosa, common but could be absent, variable friable mucosa, gross ulcerations
Surgical therapy	Total colectomy is curative	Post-operative recurrence is very high

Source: Medicine. Scientific American, 1995

Situation Analysis Diagnosis of Crohn's Disease

- Patient history (weight loss, diarrhea, pain, fever)
- CBC (white blood cells)
- Stool sample
- Endoscopy
- Biopsy
- Radiographic (upper GI, barium enema)

Situation Analysis Delay of Diagnosis

- < 40% of patients present the first year
- Average of 5 years with symptoms before accurate diagnosis
- Average age of diagnosis - 36 years old
- Children average 12-18 months before a diagnostic test is performed

Situation Analysis Disease Etiology

The etiology of Crohn's disease is unknown, however the patients tend to have the following characteristics:

- ✓ Gender - females > males
- ✓ Age - Highest incidence between 25-35 years old
- ✓ Race - Jews > Non- Jews > Blacks
- ✓ Geographic - Westernized, northern countries
- ✓ Family - Approximately 20% first degree relative with IBD

Source: J.B. Kilsner, Inflammatory Bowel Disease

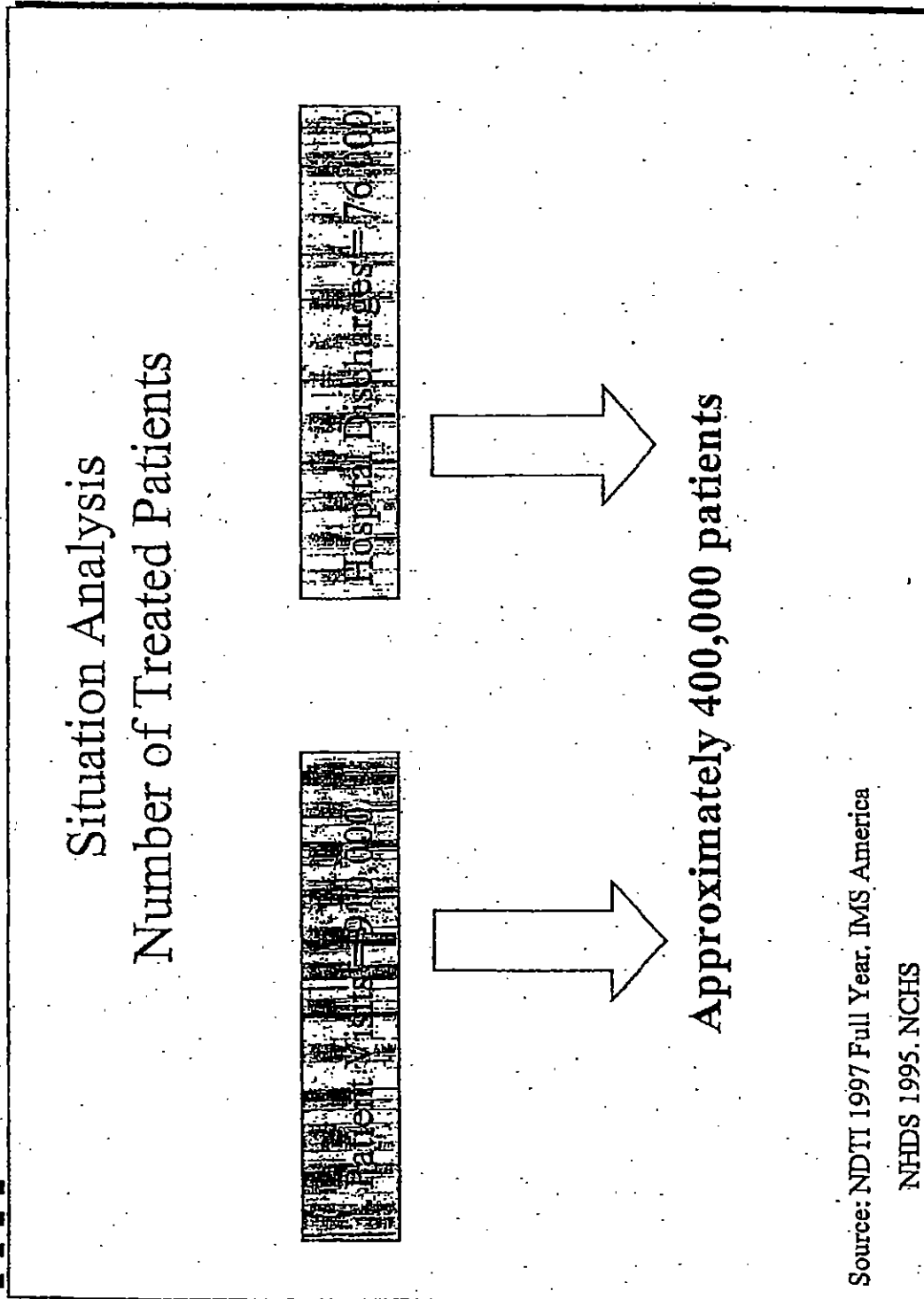
Market Overview Disease Epidemiology

Total patients afflicted with disease is unclear due to discrepancies in audits and reported incidence/ prevalence figures

- ✓ Patient awareness
- ✓ Physician training
- ✓ Diagnosis difficulty
- ✓ Incomplete study population
- ✓ Study densities

Result: Report patients between 250,000 - 800,000

Source: J.B. Kirsner, Inflammatory Bowel Disease

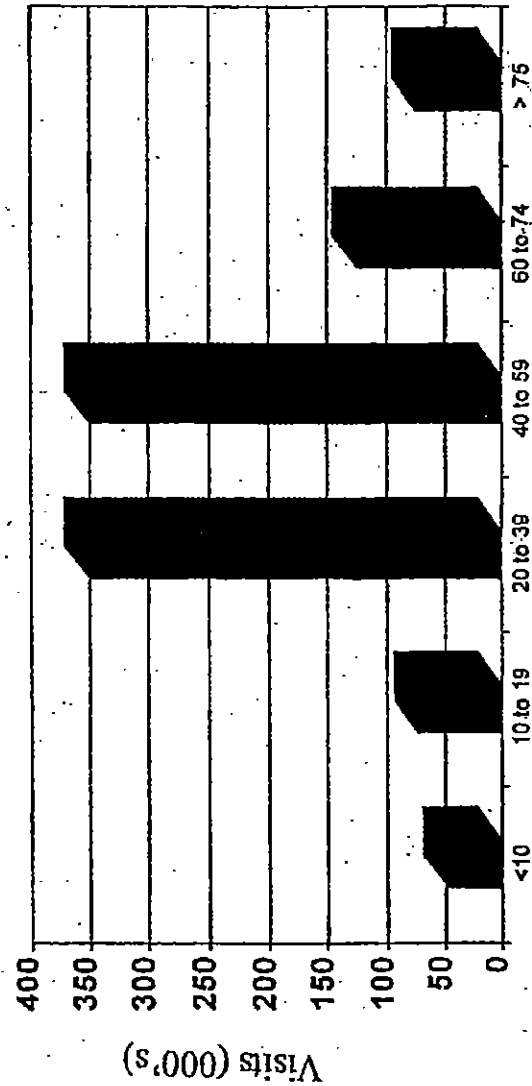


Situation Analysis Crohn's Patient Profile

- Age
- Gender
- Location of visit
- Number of visits
- Specialty
- Disease severity

Situation Analysis Crohn's Patient Profile

Age Distribution of In-Office Patient Visits

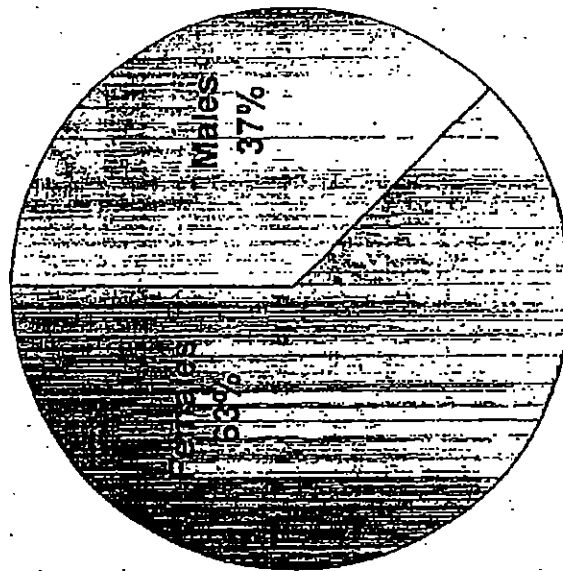


n = 910,000

Source: NDTI, Jan. 97- Dec. 97. IMS America

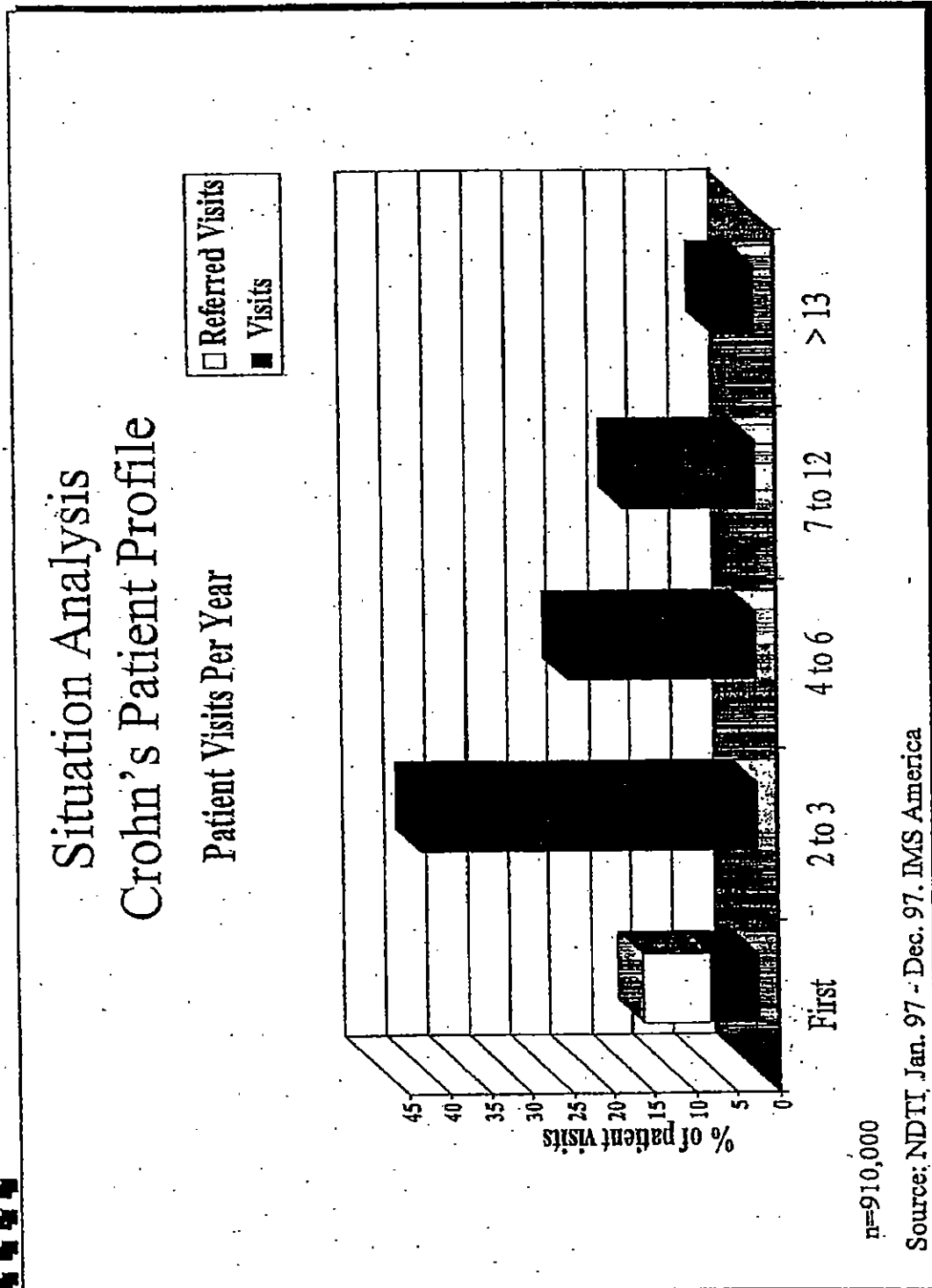
Situation Analysis Crohn's Patient Profile

Patient Gender By Office Visits



n = 910,000

Source: NDTI Jan. 97 - Dec. 97, IMS America



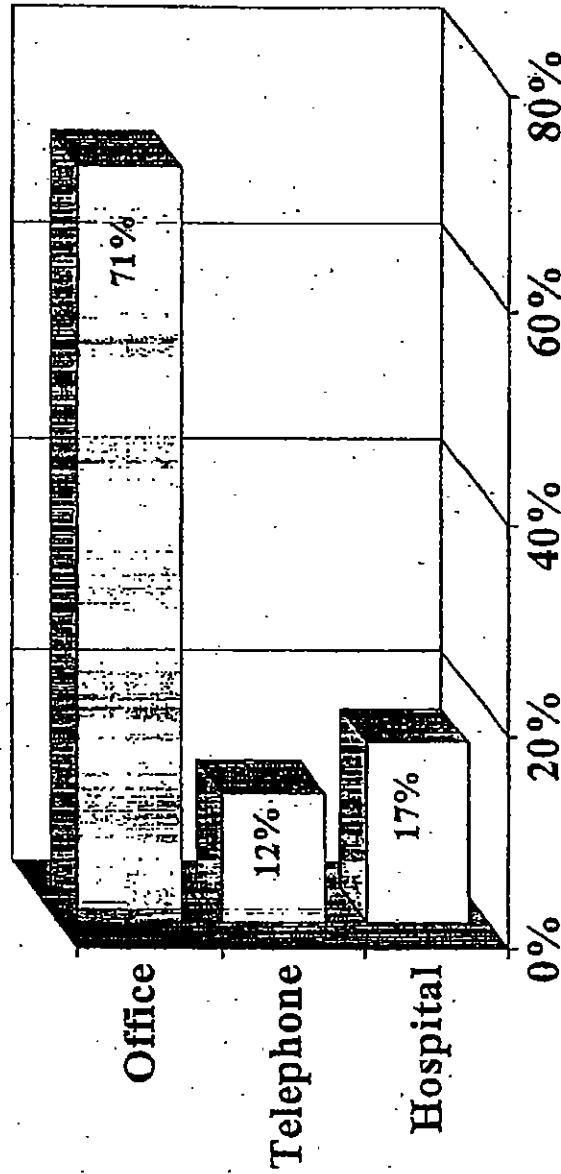
Situation Analysis Crohn's Patient Profile

- Average of 3.7 office visits per year
- Over 40% see their physician 4+ times per year
- Over 50% of first time visits are referrals
- Average of 13.3 days lost per year from work

Source: J. Kurate, Gastroenterology 1992; 102:1040-1948

Situation Analysis Crohn's Patient Profile

Location of Visit

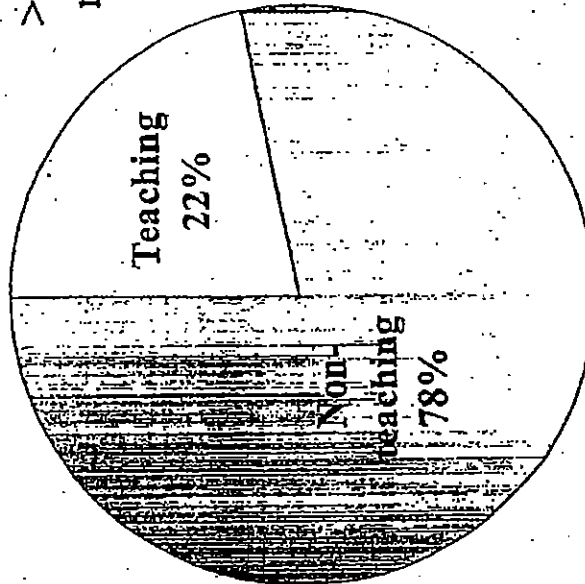


n = 910,000

Source: NDTI America Jan. 97 - Dec. 97. IMS America

Situation Analysis Crohn's Patient Profile

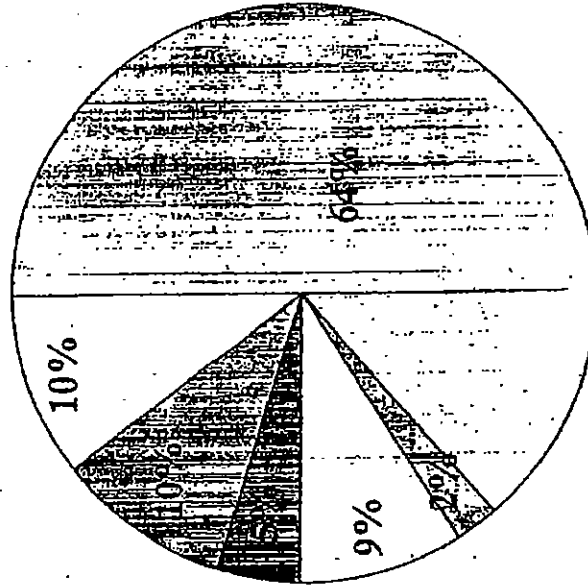
> 83% discharges in
major MSA setting



76,000 Hospital Discharges

Source: NCHS, NHDS 1995.

Situation Analysis Physician Specialty Consulted

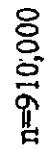


- ☐ Gastroenterology
- ☐ Colorectal Surg.
- ☐ General Surg.
- ☐ FP/GP
- ☐ IM
- ☐ All Other

n=910,000

Source: NDTI Jan 97-Dec 97. IMS America

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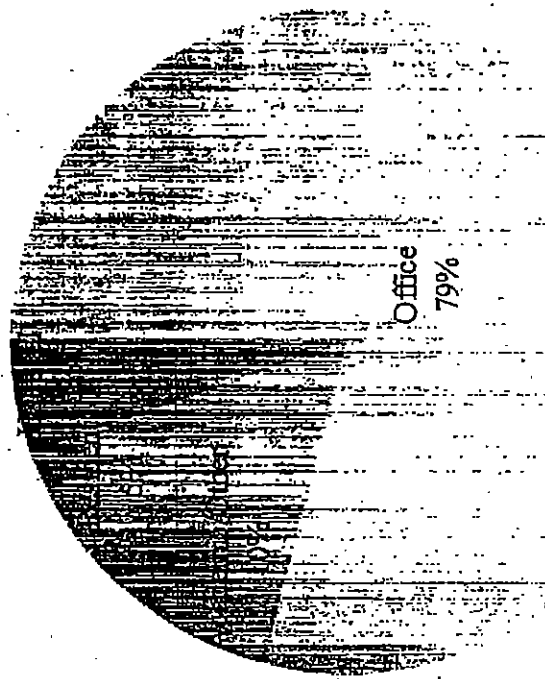


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Market Overview Gastroenterology

- Distribution
- Specialty Diagnosis Visits
- Targets
- Location
- Type of practice
- Practice profile

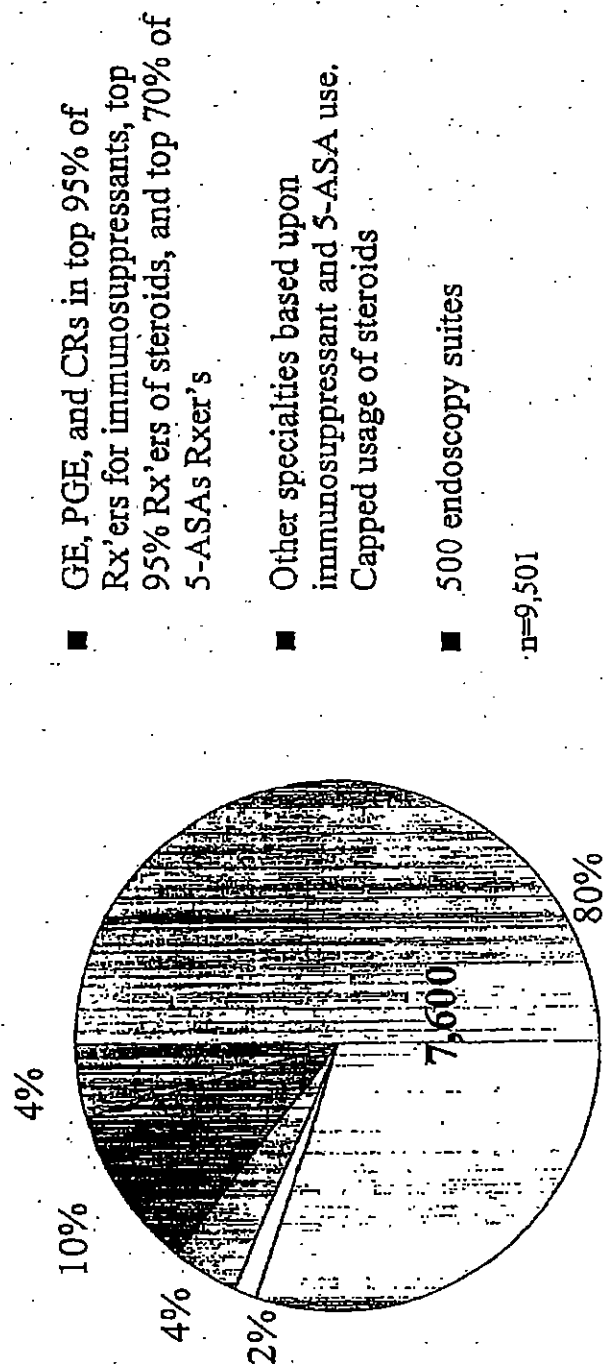
Situation Analysis
Distribution of Gastroenterologists
Location of Practice Setting



n = 9,404

Source: Source Informatics, 1997

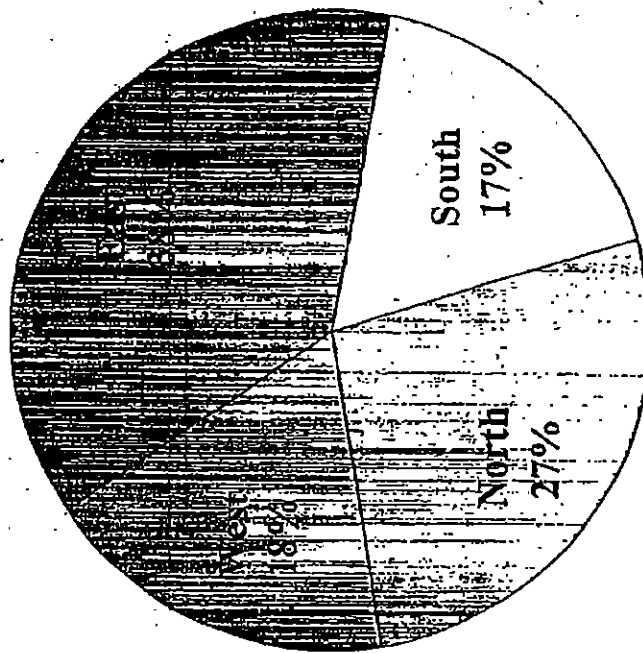
Situation Analysis Gastroenterology Targets



☐ GE
 ☐ PGE
 ☐ CR
 ☐ IM
 ☐ Other

Source: Team Analysis, ZS Assoc.,

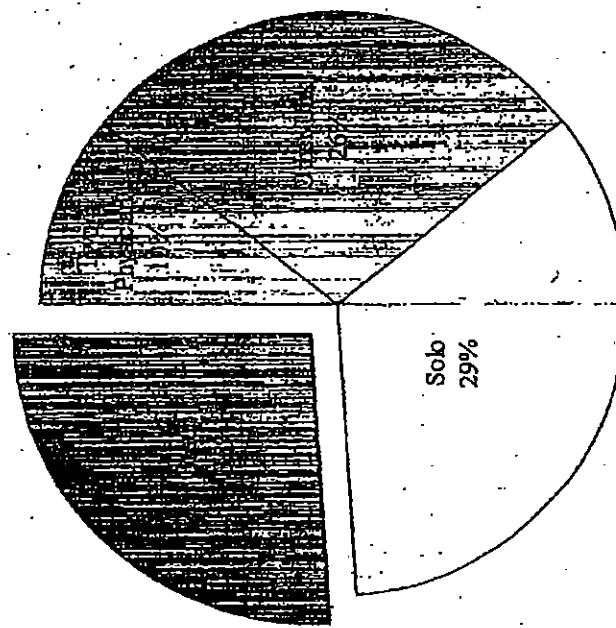
Situation Analysis
Distribution of Gastroenterologists
Across the United States



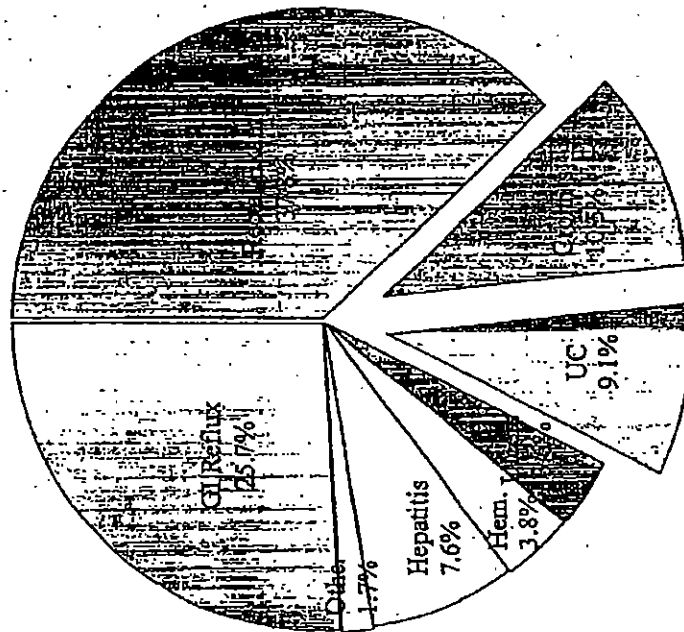
n = 6,732

Source: NDTI 1997. IMS America

Situation Analysis Distribution of GEs By Practice Type



Situation Analysis Gastroenterology Diagnosis Visits



n = 4.8mm

Source: NDTI Dataview 1997. IMS America

Situation Analysis Practice Profile

Profile Parameter	Average Gastroenterologist	Average for all Other Physicians
Patient visits/work day	10.8	13.0
Rx's per work day	12.3	15.4
Drugs per patient visit	1.2	1.2
Location of Patient Visits		
Office	65%	84%
Hospital	26%	10%
Phone	7%	5%
Referred patients	75%	23%
Visits with drugs	60%	68%
Visits without drugs	40%	32%

Source: NDTI 1997. IMS America

Situation Analysis Treatment

- Pharmacological
- Nutritional support
- Surgical

Situation Analysis Pharmacologic Options

■ Aminosalicylates

- sulfasalazine (AZULFIDINE®)
- 5-ASA/mesalamine (ASACOL®, PENTASA®, ROWASA®)
- 5-ASA/olsalazine (DIPENTUM®)

■ Corticosteroids

- various oral generics
- Solu-Medrol®, injectable

Situation Analysis Pharmacologic Options

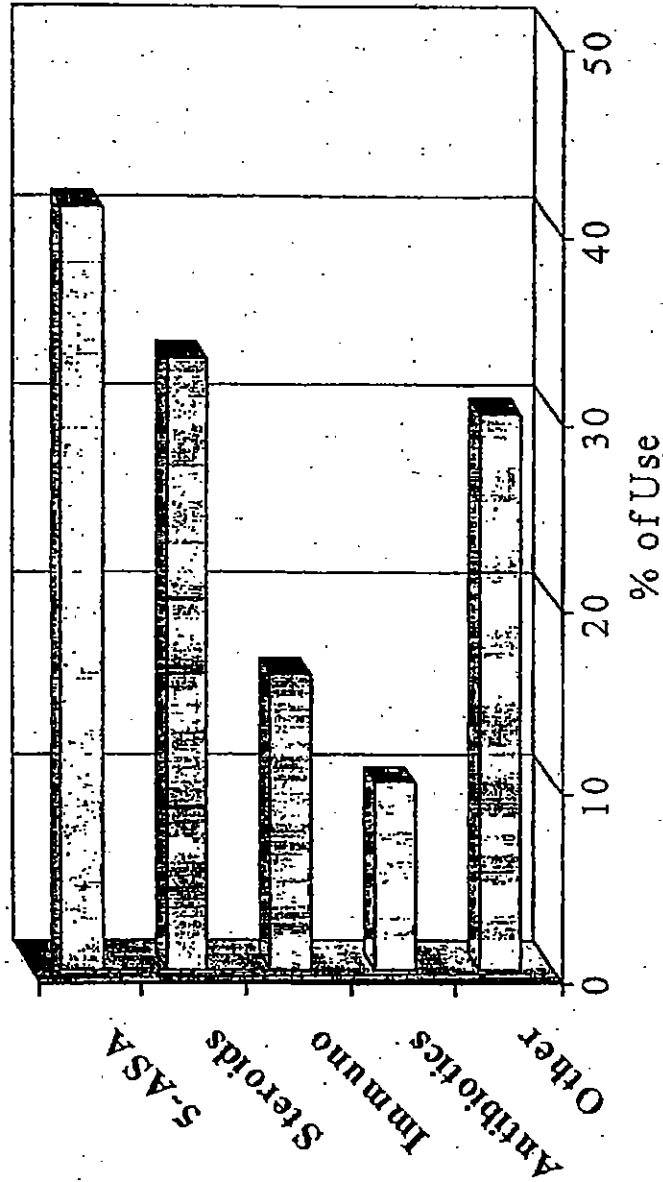
■ Immunomodulators

- azathioprine (IMURAN[®])
- 6-mercaptopurine (PURINETHOL[®])
- Cyclosporine
- Methotrexate

■ Antibiotics

- metronidazole (FLAGYL[®])
- Ciprofloxacin (CIPRO[®])

Situation Analysis Drug Uses

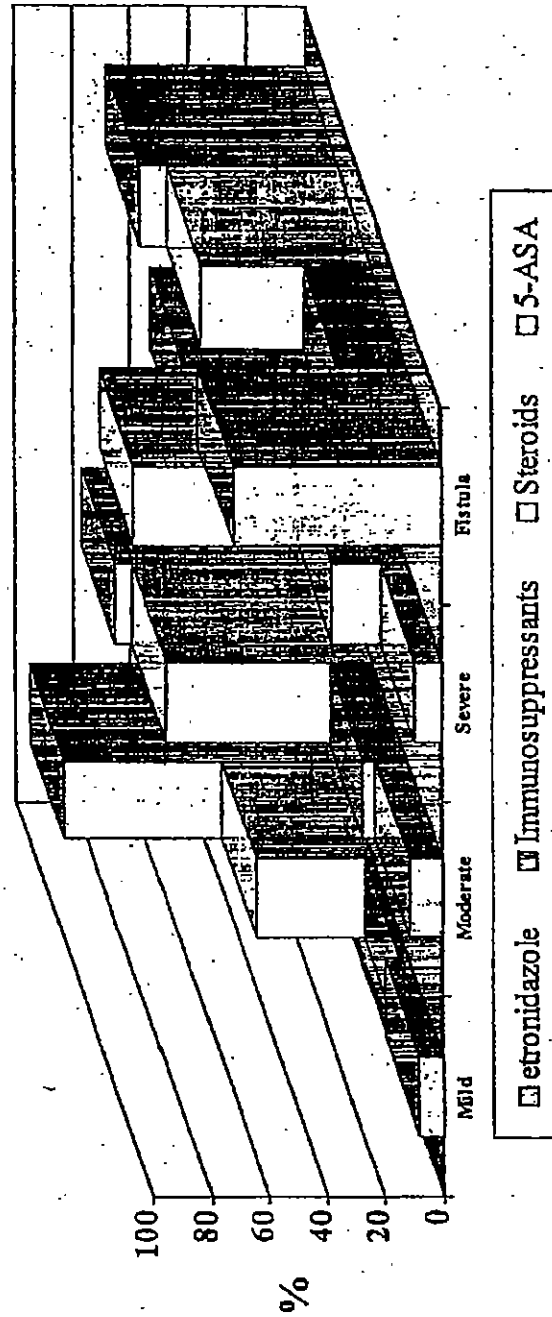


Total Uses = 1,065,000. Note: Percents add to greater than 100% due to multiple therapies

Source: NDTI Jan. 97 - Dec. 97. IMS America

Situation Analysis Commonly Used Drugs in Crohn's Disease

% of Patients by Severity of Disease



Source: Profile of Current Knowledge, Attitudes and Practices of Gastroenterologists Relative to the Treatment of IBD. Mattson Jackson Group, St. Louis, 1995 and NDTI 1997. IMS America

Situation Analysis Other Therapies

- Surgery, 60% of patients within 10 years
 - Bleeding
 - Obstruction
 - Abscess
- Nutritional therapy - malabsorption
 - Liquid
 - Total parenteral nutrition (TPN)
 - Enteral nutrition (EN)

Source: Immune Disease, DR Report 1997

Situation Analysis Future Competition

- Late Stage Developments
- Comparisons to cA2

Situation Analysis Pipeline

Class	Product	Status	Manufacturer	Indications
Anti-sense	ISIS 2302	Phase II Potential entry 2000	ISIS Pharmaceutical w/Boehringer Ingelheim	Crohn's, transplantation
Anti-TNF	CDP571	Phase II Potential entry 2000	Celltech	Septic Shock Phase III, RA and CD Phase II
Anti-inflammatory cytokines	IL-10	Phase III Potential entry 2000	Schering-Plough	Crohn's, early phase RA

Situation Analysis Pipeline Commentary

Product

Comments

ISIS 2302

- Steroid dependent patients
- Not quite as efficacious
- IV daily infusions

CDP 571

- Comparable efficacy
- Milder patients in studies
- mg/kg, not as effective
- Humanized
- IV

IL-10

- Short half life, 2-6 hrs
- IV daily infusion; potentially SQ
- Neutropenia
- CRP transient effect

Situation Analysis Summary

- Market estimates place CD prevalence at 400,000 individuals
- CD is a lifelong affliction impacting patients overall well-being and quality-of-life
- CD is difficult to diagnose and manage
- Over 40% of patients see their physician 4+ times per year
- Over 70% of patients have moderate-to-severe disease

Situation Analysis Summary (cont'd)

- Gastroenterology is the primary specialty consulted and referred to for Crohn's disease
- Centocor's targeted gastroenterologists are high volume prescribers of agents utilized in the management of CD
- Selling efforts will need to be focused on the office, but the hospital should not be neglected
- Pharmacologic agents, nutritional support, and surgical intervention provide treatment options but do not provide the optimal therapy
- Newer agents that may compete with cA2 might enter the market as early as 2000

Situation Analysis Cost of Illness

- Publications are very limited
- Key citation: Hay and Hay, annual direct cost \$6,561 (1990)
 - Equivalent to \$9,197 in 1996 dollars (medical CPI)
 - Surgical Interventions 46%
 - Medical inpatient interventions 34%
 - Medications 10%
 - Other 10%
 - Total 100%
- University of Chicago hospitalization charges (1996-97)
 - Average length of stay: 7.6
 - Mean charge \$27,433, median charge \$21,127

cA2 Marketing Plan Payer Situation Analysis

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Payer Situation Analysis Background

- A favorable payer environment is critical to marketing success
- The policies and procedures that payers adopt to manage a new agent can either positively or negatively impact sales
- Although cA2 is
 - a breakthrough therapy for a relatively small patient population
 - its novel nature and relatively high cost will trigger payer scrutiny
- Data to support a cost effectiveness or cost offset claim will not be available at launch

Payer Situation Analysis Background

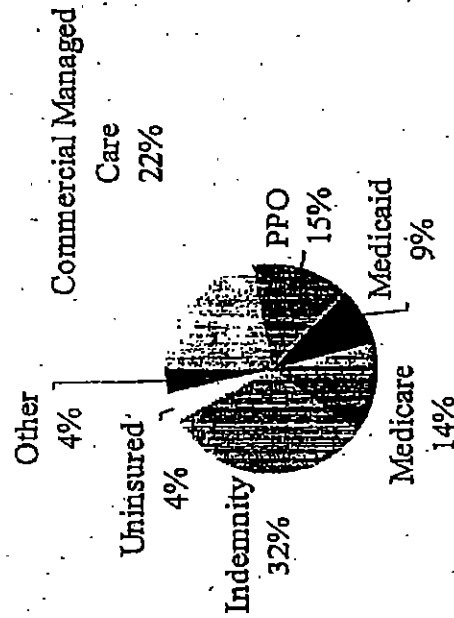
Payers Affect Market Adoption in Two Ways- Access and Financing

- Patient access to
 - Specialty care - referrals to gastroenterologists
 - Treatment settings - hospitals, offices, clinics, etc
 - cA2 treatment - usage constraints
- Provider financing
 - Incentives - Positive margins on drug reimbursement increases net income and facilitates adoption
 - Disincentives - Capitated contracts or negative margins on drug reimbursement decreases net income and impedes adoption

Payer Situation Analysis Background

Although the U.S. population is rapidly migrating to managed care, indemnity insurance is likely to be the dominant payer at launch

Crohn's Disease Payer Mix



- However, the federal government and most states are transitioning to managed care
- 10% of Medicare and 40% of Medicaid covered lives are currently in a managed plan

Payer Situation Analysis Key Issues-Indemnity/PPO Insurance

- Few restrictions placed on provider choice, treatment setting or therapy
- Generally favorable reimbursement
 - Fee-for-service or discounted fee-for-service (PPO)
- Off-label coverage policy will be favorable, but may require negotiation with individual carriers
 - Publications and pharmacy reference compendia citations are needed to document medical necessity
- Assumptions
 - Reimbursement rate \geq 95% of AWP
 - Ancillary infusion service will be reimbursed \$30-\$40 per encounter
 - PPO provider networks will include a sufficient number of pro-cA2 gastroenterologists

Payer Situation Analysis Key Issues-Managed Care

- Effective management of medical costs is one of the primary drivers of managed care organization (MCO) stock price
- Health plans manage medical costs by
 - Shifting risk to a contracted provider via
 - » Prospective payment agreements (capitation)
 - » Case rate reimbursement
 - » Per diem reimbursement
 - Bearing risk with the concomitant use of "control mechanisms" to discourage unnecessary utilization of expensive technologies

Payer Situation Analysis Key Issues-Managed Care (cont.)

There are two types of control mechanisms-explicit and implicit

- Explicit (drug or disease-based)
 - » Formularies
 - » Clinical practice guidelines
 - » Case management, etc.
 - Example
 - » Clinical practice guideline requires failure on low cost steroids and immunosuppressants before authorizing cA2

Payer Situation Analysis Key Issues-Managed Care (cont.)

There are two types of control mechanisms-explicit and implicit

- Implicit (financial or system-based)
 - » physician cost profiling
 - » gatekeeper physician referral requirements
 - » reimbursement withhold contracts, etc.
- Example
 - » physician cost profiling might threaten a high-cA2 prescriber with plan de-selection at contract renewal

Payer Situation Analysis Key Issues-Managed Care (cont.)

The FDA-approved indication will be a key determinant of managed care resistance

- Typically, there is no legal requirement to cover uses outside of the FDA approved indication for non-oncology drugs
- New use coverage may be possible via negotiation and documentation, but success is not guaranteed
- A narrow indication (fistula only) will increase resistance
- A broad indication (moderate-severe non-fistula) will reduce, but not eliminate overall managed care resistance

Payer Situation Analysis Key Issues-Managed Care (cont.)

Summary Assumption: Managed care will create significant resistance to full adoption, but the impact will take many forms

- Control mechanisms will vary widely (>20 different types)
 - Policy is typically established at the health plan level; rarely at MCO corporate
 - Constraints will range from modest to severe
 - » Modest - require a letter of medical necessity
 - » Severe - denial for non-fistula use
- Control mechanisms may impact any or all three revenue drivers
 - Patient selection (penetration)
 - Dosing (vials/patient)
 - Re-treatment frequency (infusion/year)

Payer Situation Analysis Key Issues-Medicare

- Drug coverage is contingent upon
 - Medical necessity
 - An FDA approved use
 - Administration site that is "incident to a physician's services"
 - » Hospital- or office-based administration will be covered; home care will not
- Covered amount will be 95% of AWP
 - HCFA will reimburse the provider 80% of 95% of AWP
 - The patient/secondary insurer is responsible for other 20%
- Coverage of uses outside of the approved indication is negotiated with individual HCFA carriers and will require peer reviewed publications for approval

Payer Situation Analysis Key Issues-Medicare (cont.)

- Effective January 1, 1999 a new hospital outpatient payment system will be implemented - Ambulatory Patient Groups (APG)
 - Prospective payment system similar to inpatient DRGs
 - The impact on cA2 is uncertain
 - BIO and Pharma are consolidating lobbying efforts to secure a carve out for expensive pharmaceuticals
- Assumptions
 - Office-based administration will be a viable treatment setting
 - Off-label coverage will be favorable after negotiation
 - Lobbying efforts will be successful in resolving the APG threat

Payer Situation Analysis Key Issues-Medicaid

- HCFA mandates drug coverage for medically accepted indications
 - Policy is administered at the state agency level
- Reimbursement is discounted fee-for-service
- Providers limited to those willing to accept the fee schedule
- Fee-for-service patients will be covered under
 - Physician benefit (office-based administration)
 - Hospital benefit (outpatient clinic administration)

Payer Situation Analysis Key Issues-Medicaid (cont.)

- The Medicaid population is rapidly transitioning from fee-for-service to managed care
 - By 2000, 70% of Medicaid covered lives will be enrolled in managed Medicaid plans
 - Managed Medicaid patients will be subject to the same constraints as non-managed Medicaid care patients
- Assumptions
 - Reimbursement rate \geq 90% of AWP
 - There will be sufficient numbers of GE's who accept the Medicaid fee schedule to serve the population

Payer Situation Analysis Summary

- Indemnity/PPO and Medicaid will be favorable assuming compedia documentation is available to support new uses
- Medicare will be favorable assuming the APG situation is resolved and office-based administration is facilitated
- Managed care will be the most problematic payer
 - The FDA approved indication will be a key factor
 - The variability of MCO control mechanisms precludes a single marketing strategy

cA2 Marketing Plan
Product Overview

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MDL-CEN00002772

Product Overview

- Anti-tumor necrosis factor alpha antibody
- Human/chimeric monoclonal antibody
- Binds and neutralizes soluble and membrane-bound forms of TNF α
 - TNF α is a key inflammatory mediator

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MDL-CEN00002773

Product Overview

Indications:

- Treatment of patients with Crohn's disease to:
 - Reduce the signs and symptoms in patients with moderate-to-severe disease activity in whom conventional therapies are inadequate
 - Close enterocutaneous fistulae

Product Overview

Dosage and Administration

- Moderate-to-severe disease:
 - Single infusion of 5mg/kg (in responders, up to 4 infusions given at 8-week intervals to sustain clinical benefit)
- Fistulizing disease:
 - Three infusions of 5mg/kg at 0, 2, and 6 weeks

Product Overview

Clinical Efficacy

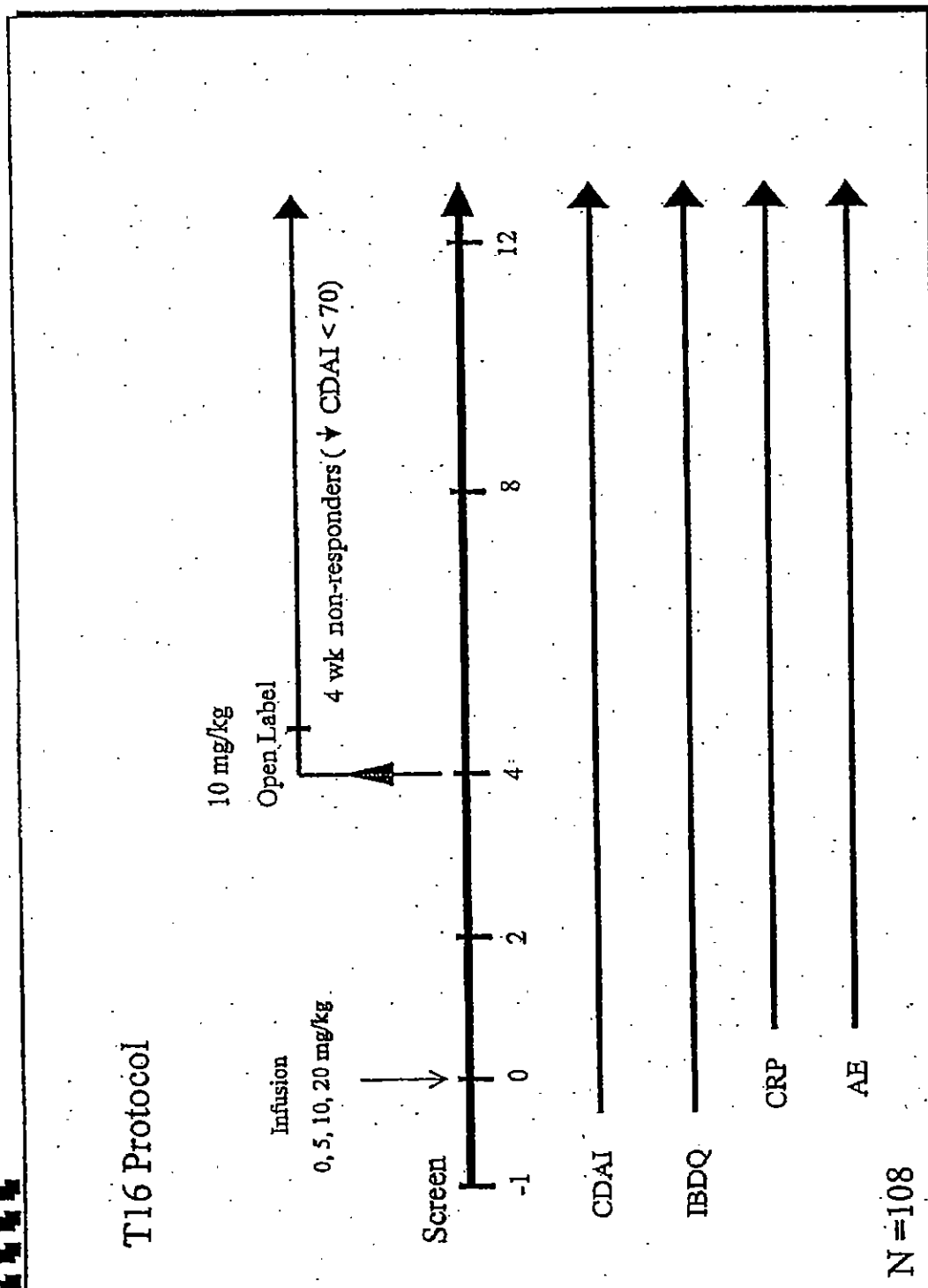
- Total of 14 studies and 627 patients
 - ATTRACT trial 450 patients
 - ACCENT trial 400 patients
- Four studies in Crohn's disease patients
- 233 patients in Crohn's trials
- Additional trials in RA, sepsis and UC
- Two pivotal Crohn's trials
 - T16 (moderate-to-severe disease)
 - T20 (fistulizing disease)

Product Overview

T16 Review

■ Treatment and retreatment

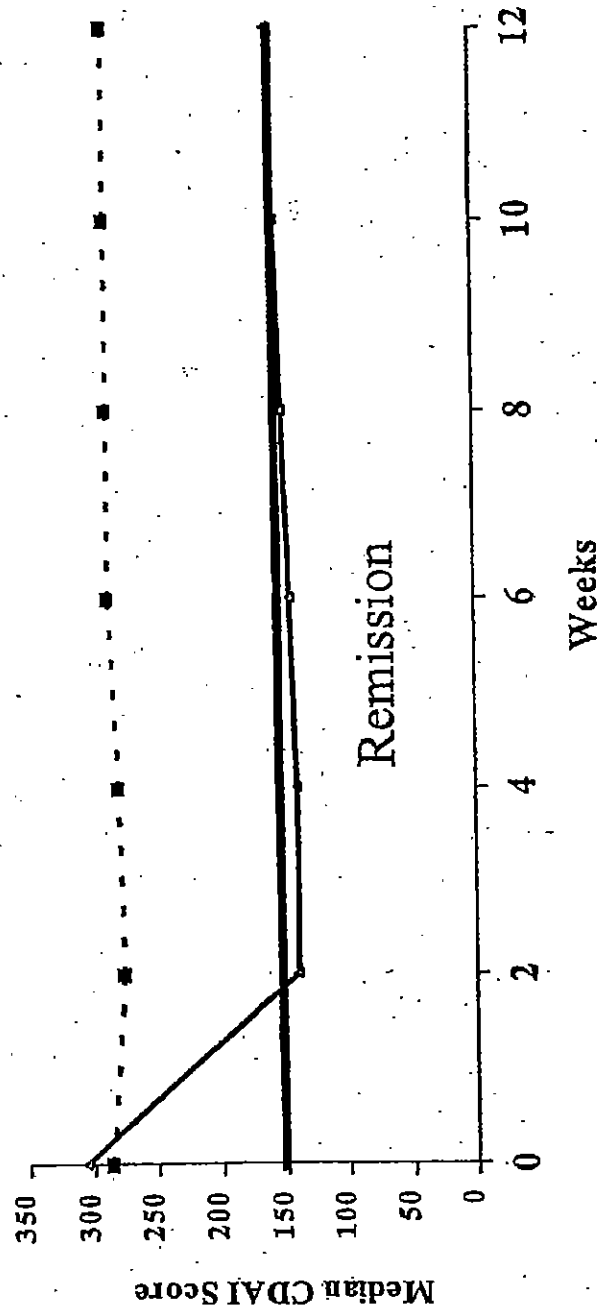
- Protocol
- Response rates
- Remission
- Crohn's Disease Activity Index (CDAI)
- Inflammatory Bowel Disease Questionnaire (IBDQ)



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Product Overview

—○— cA2 - ■ - Placebo



Remission

Median results for the CDAl in patients who had a clinical response. Multicenter, randomized, placebo-controlled, double-blind trial. Clinical response was considered a 70-point reduction in the CDAl score from baseline mean score of approximately 300. CDAl score below 150 indicates remission; scores above 450 indicates severe illness. Placebo patients were maintained on their current therapy throughout the trial.

*P=.059

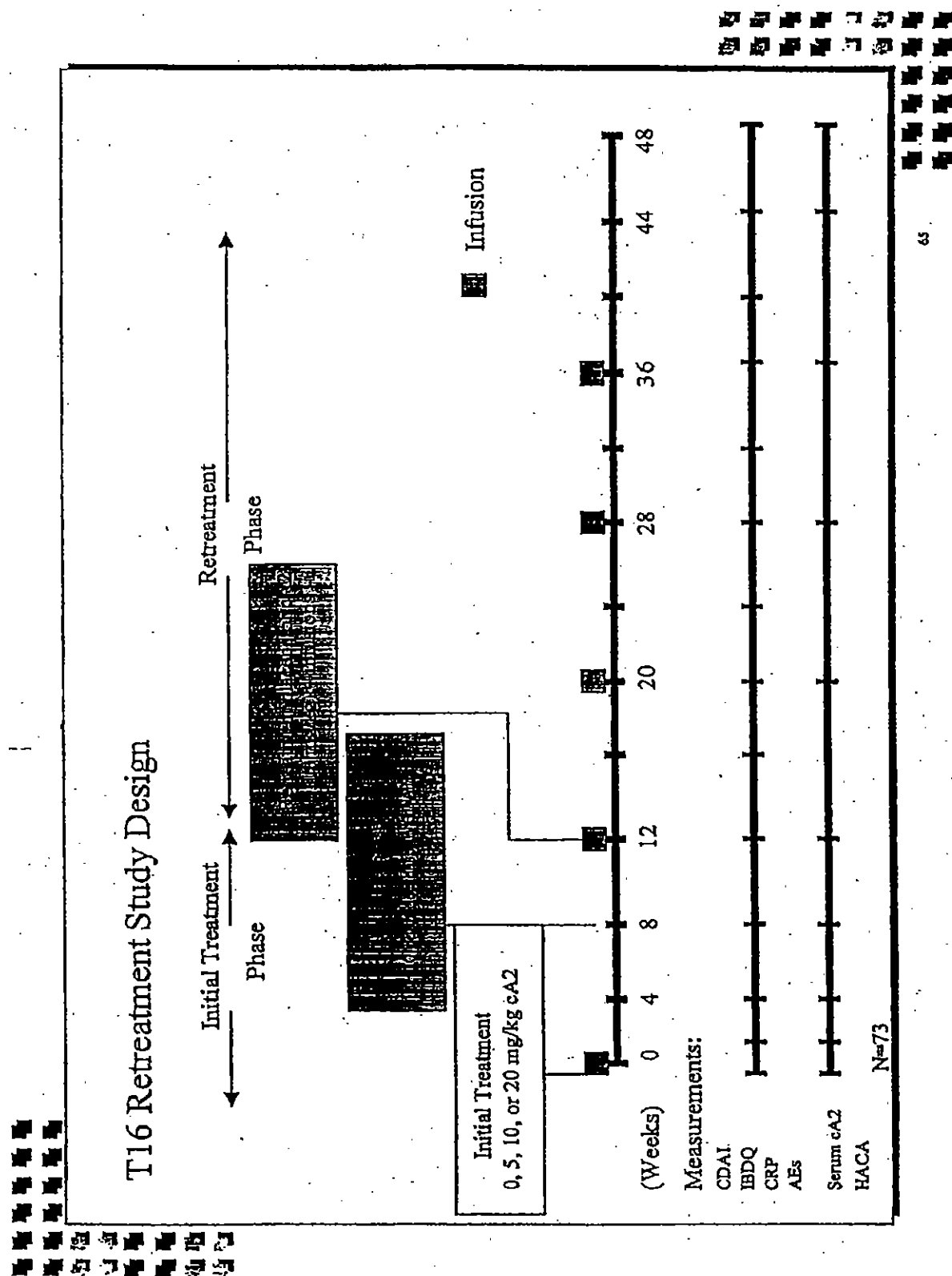
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Product Overview

T16 Initial Treatment Phase (N=107)

- 1 of 2 pivotal trials supporting the BLA
- Single infusion protocol
- Placebo patients had background therapy



Product Overview

T16 Retreatment Phase (N=73)

- Responders to initial and open label treatment received additional infusions (at 12, 20, 28, 36 weeks)
- Retreatment with cA2 every 8 weeks maintained the initial treatment benefit on the 48 week study period
- Study supportive of the BLA
- Repeat dosing data expected to be included in final P.I. but not acknowledged indication

Product Overview

T20 Review

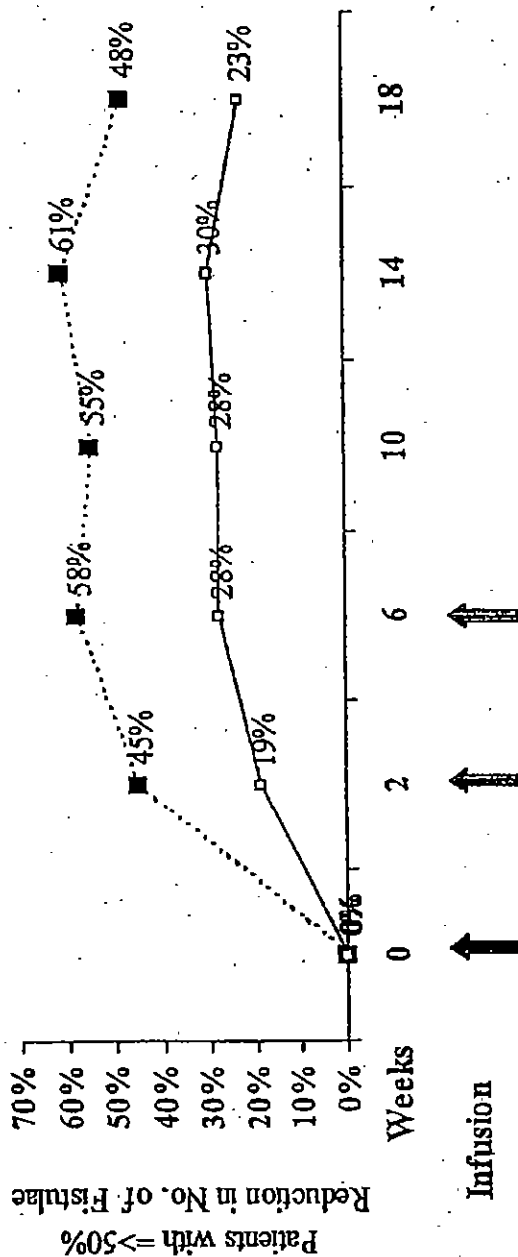
- Fistulizing disease
 - Protocol
 - Primary endpoint
 - Complete response

Product Overview

- Patients with single or multiple enterocutaneous fistulae
 - 94 patients (0, 5 or 10 mg/kg) of cA2
 - Draining at least 3 months
 - Concurrent therapies permitted
 - Patients received three infusions and were followed for 18 weeks
- Primary endpoint
 - $\geq 50\%$ reduction in the number of open fistulae for at least two consecutive evaluation visits (i.e. at least 1 month)

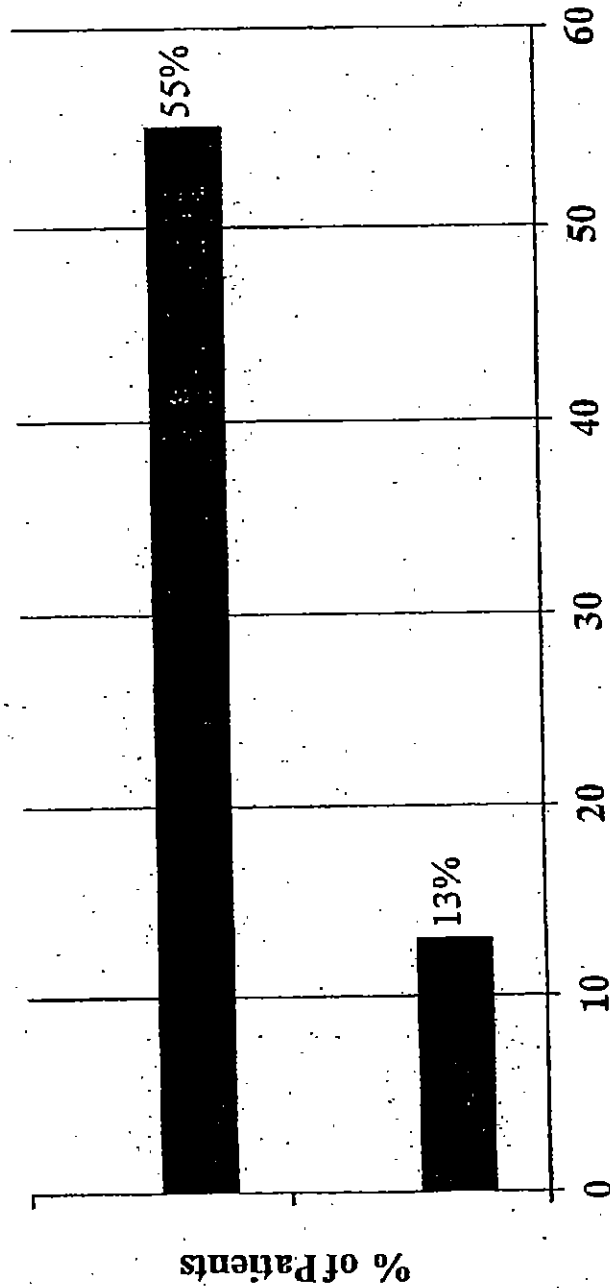
Product Overview T20 Fistula Trial

---■--- cA2 5mg/kg —□— Control



Number of patients achieving a >50% reduction in the number of draining fistulae at each evaluation visit. Results over 18 weeks with cA2 5mg/kg at 0, 2, and 6 weeks

Product Overview
Majority of cA2 Patients Achieved
Completed Closure of all Fistulae



Product Overview Safety

The following table summarizes the most frequent reasonably related adverse events:

	Control*	cA2
Patients evaluated	n=109	n=453
Average weeks of follow-up	12.2	22.3
% of patients with any adverse experiences	29.4	47.5
Headache	9.2	9.9
Nausea	3.7	6.2
Pruritus	0.9	4.4
Dizziness	5.5	4.4
Fatigue	1.8	4.2
Fever	2.8	4.2

*Patients in the control group were receiving background therapy including one or more of the following: aminosalicylates, corticosteroids, immunosuppressants, and antibiotics.

†The cA2 treatment group includes patients from Crohn's and non-Crohn's clinical trials involving single and multiple infusions.

cA2 Marketing Plan Safety

■ Infection

Issue: Anti-TNF agents theoretically influence ability to mount appropriate inflammatory response

- Infection rate in cA2 patients similar to placebo
- Although clinical significance appears minimal, physicians unfamiliar with cA2 may be concerned with the risk to patients

cA2 Marketing Plan Safety

■ Lymphoma

Issue: 4 patients in clinical trials developed lymphomas

- Patients with RA and Crohn's disease with long histories and chronic exposure to immunosuppressant therapies
- Gastroenterologists are aware of reported lymphomas and will be concerned with the risk to patients
- The incidence is within the expected range

Product Overview cA2 Safety Summary

Lymphoma Case Histories:

Patient	Disease /Duration	Prior or Concomitant Immunosuppressive Therapy	Infliximab Dose Initial	Infliximab Dose Recurrence	Classification	Latency
61 yr old male	CD ⁺ 30 years	Azathioprine, prednisone	10 mg/kg	placebo (1x)	B-cell lymphoma	9.5 months
48 yr old male	RA/ 16 years	Azathioprine, prednisone, MTX	10 mg/kg	10 mg/kg (1x)	B-cell lymphoma	18 months
61 yr old male	RA/ 16 years	MTX	1 mg/kg	N/A	Hodgkins lymphoma	6.5 months
36 yr old male	AIDS/ unknown	N/A	10 mg/kg	10 mg/kg (1x)	B-cell lymphoma	9 months

Clinical data on file as of 4Q97

067397.1McGowan

Product Overview Safety

Immunogenicity

- Human anti-chimeric antibodies (HACA) have been observed in patients treated with infliximab
- The incidence of HACA formation is approximately 10% or less in current doses under development
- There is a potentially higher incidence of infusion reactions in patients who develop HACA
 - there have been HACA (+) patients with multiple infusions with no clinical diminished efficacy nor infusion reactions noted
 - ongoing trials will further study the significance, if any, on HACA formation

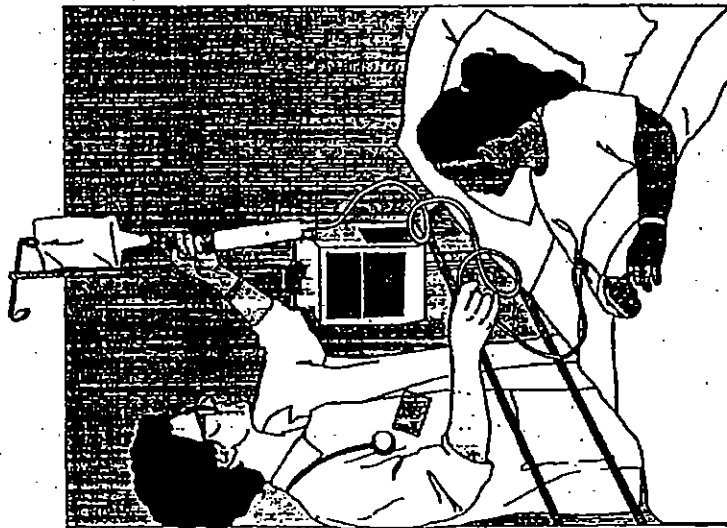
Clinical data on file as of 4Q97

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cA2 Marketing Plan Infusion Reactions

Infliximab (anti-TNF α) Administration

- Infusion reactions are occasionally observed with retreatment
- Symptoms may include: fever, headache, nausea and rash
- Most reactions respond to slowing the infusion rate and/or medical treatment with antihistamines and/or acetaminophen



Product Overview Infusion Reaction

Infusion - Related Events*

Nonspecific reactions	4.8%
Pruritus or urticaria	1.2%
Cardiopulmonary reactions	1.5%
Cardiopulmonary and pruritus/urticaria	0.2%

*1207 total infusions

cA2 Marketing Plan Infusion Requirements

■ Infusion Supplies

- Non-PVC IV tubing with 1.2 μ filter & rate control device
- Non PVC administration bag or glass bottle
- Sterile water for injection & sodium chloride for dilution
- IV catheter
- Syringes
- IV starter kit

■ Administration Procedure

- Preparation
- Infusion
- Monitoring

cA2 Marketing Plan GE Reactions to Concept

- Unmet clinical needs
 - Satisfaction with current treatment is low
 - » Efficacy in severe disease is less than satisfactory
 - » Immunosuppressants have a long onset of action and increase risk of infection, cancers and pancreatitis
 - » Corticosteroids are effective but cannot be used for long-term therapy because of side effects
 - Clear need for newer agents that
 - » Are more efficacious
 - » Have more rapid onset of action
 - » Have fewer side effects

Source: Brintnall & Nicolini, April 1997

cA2 Marketing Plan GE Reactions to Efficacy

- Reactions to cA2 were strongly positive
- Reasons cited:
 - Unique mechanism of action
 - High response rates
 - Quick onset of action
 - Efficacy in patients with fistulae (difficult-to-treat)
- Infusion method of administration is cited as an obstacle to use

Source: Brintnall & Nicolini, April 1997

cA2 Marketing Plan Place in Treatment Algorithm

- Patient types mentioned by GEs
 - Initial therapy
 - » Patients with fistulae (n= 80,000 pts)
 - Reserve for:
 - » Moderate-to-severe patients still uncontrolled on conventional therapies (n= 100,000 pts)
 - » Steroid-dependent patients (n= 60,000 pts)
 - » Alternative to immunosuppressants where side effects are a concern (n= 20,000 pts)
- Establishing place in current treatment critical to acceptance
- ACG guidelines

CA2 Marketing Plan Management of Crohn's Disease in Adults

Signs and Symptoms

- Chronic or nocturnal diarrhea
- Abdominal pain
- Evidence of obstruction weight loss, fever or other symptoms reflecting an underlying inflammatory, fibrotic, or fistulizing process

History, Physical Exam, and Lab

Confirm Diagnosis

Determine Disease Location

Determine Disease Severity

Endoscopic Confirmation

- Upper or lower GI endoscopy to confirm diagnosis, assess disease location, or obtain tissue for evaluation
- Colonoscopic evaluation of surgical anastomosis to predict likelihood of recurrence
- Endoscopic biopsy to establish diagnosis, rule out acute self-limited colitis, or identify dysplasia or cancer

- Radiological Confirmation
- Contrast Radiography
- Small Bowel Enteroclysis
- Abdominal or Transrectal Ultrasonography
- CT or MRI

Mild to Moderate

Moderate to Severe

Severe to Fulminant

Weaknesses

- cA2 is a new class of drug - natural "wait and see" attitude
- cA2 might only be approved for fistulizing Crohn's disease, which will increase payer use restrictions
- If initial indication is limited to fistulae only, a second biologic might enter the market with a broader indication before cA2 gets expanded labeling (late 1999/ early 2000)
- cA2 is potent inhibitor of TNF- α which raises physician concern about infection and lymphoma
- Formation of HACA raises some concern among some customers

Weaknesses

- cA2 initial indication will be for "acute" treatment. Questions about repeat dosing will be prevalent
- cA2 route of administration will add to end user costs associated with the treatment
- IV route of administration is uncommon in Gastroenterologists' offices
- No definitive cost-effectiveness data at launch
- Centocor is not well known among Gastroenterologists
- Manufacturing response time to greater than expected demand

Opportunities

- Low competitive intensity in the Crohn's therapeutic area
- cA2 use in less severe patients is likely to develop over time
- Increased chronic cA2 use with the maintenance indication (2001)
- cA2 will be the first TNF-inhibitor biologic approved in any therapeutic class

Opportunities

- IBD market potential is highly concentrated among approximately 7,500 key GEs
- Recent FDA new-use promotion guidance (early 1999)
- Potential cA2 spill-over into severe ulcerative colitis treatment
- cA2 likely to be more convenient (fewer injections or infusions) and less expensive than emerging biologic competitors

Opportunities

- Small Crohn's disease patient population and cA2 orphan drug status may limit payers' price sensitivity
- Given symptomatic nature of disease, patient influence will be key driver of cA2 demand both with providers and payers
- Crohn's patients are well organized and networked. CCFA can help drive patient awareness of cA2 availability and break down access barriers
- Crohn's disease diagnosis often delayed or missed - market expansion

Threats

- Anti-TNF inhibition is a new class of drug - long term experience unknown
- Only a limited number of key physicians have clinical experience with cA2
- Payers likely to impose patient access restrictions to limit utilization of cA2
- More limited fistulae-only indication will lead to greater patient access restraints by payers

Threats

- Restrictive provider formularies might limit cA2 use
- Navigating through reimbursement mechanisms introduces a nuisance factor in using cA2
- Financial risk associated with performing in-office infusions might prove cost-prohibitive for some physicians

Threats

- Gastroenterologists under a specialty capitation will have disincentive to use cA2
- Physicians likely to experiment with dose and dosing regimes - clinical and safety consequences unknown
- Enbrel expected to be launched for RA in 1999 - possibility of new-use-label CD use
- A number of potential biologic competitors on the horizon in IBD

Key Strategic Imperatives

- Position cA2 to uniquely meet the gaps in clinical management of CD while differentiating the product from the immunosuppressant and anti-inflammatory drug classes
- Anticipate and prepare response plans to address concerns about cA2 safety, especially infection and lymphoma risk and the relevance of HACA formation
- Establish new Crohn's disease treatment goals and position these to physicians and patients:
 - rapid and sustained symptom remission
 - minimal drug-related toxicities
 - endoscopic healing and fistulae closure
 - restoration of normal quality of life

Key Strategic Imperatives

- Establish leadership position in the treatment of IBD among gastroenterologists
- Position cA2 as the first TNF inhibitor across therapeutic classes
- Position cA2's IV route of administration as patient management advantage
- Fully support in-office use of cA2 among Gastroenterologists by providing turn key services

Key Strategic Imperatives

- Leverage existing high level of cA2 awareness and interest to accelerate early adoption at launch
- Establish cA2 pricing that reflects product value yet is sensitive to overall cost to manage Crohn's disease
- Set AWP at a level that preserves a modest margin for providers, ensures break-even potential for Medicare providers, and is consistent with payer price elasticities
- Ensure payer formulary acceptance by communicating a reasonable economic rationale for cA2 price and treatment cost

Key Strategic Imperatives

- Prevent administrative burdens from negatively impacting the cA2 prescribing decision by providing reimbursement support for physicians and patients
- Work with payers to implement appropriate patient access criteria to minimize constraints placed on cA2 patient selection, dosage, and treatment frequency by working with payers to implement appropriate patient access controls while minimizing administrative burden
- Educate primary care physicians about Inflammatory Bowel Disease and its proper diagnosis. Encourage more rapid referrals to Gastroenterologists

cA2 Marketing Plan Key Strategies

HIGHLY CONFIDENTIAL

MDL-CEN00002815

Product Overview Clinical Positioning

Message Testing Findings*:

- GEs are clinically oriented and less interested in the science behind monoclonal antibodies
- Physicians are particularly interested in how cA2 improves patient quality of life
- Physicians need help in identifying appropriate patients for cA2 treatment
- Physicians do not immediately relate to CDAI and IBDQ measures

* Brintnall & Nicolini, 3/98

cA2 Marketing Plan Clinical Positioning Strategy

Objectives:

- Find a unique, memorable position that cA2 can own
- Set a new standard of care- remission level symptom control and endoscopic healing
- Establish a target patient audience consistent with the clinical data per key trial protocols
- Establish positioning that describes what cA2 does for patients (i.e. improve QOL)
- Develop positioning that can be modified to expand usage for a broader role

cA2 Marketing Plan
Positioning Statement

"cA2 is a new standard of treatment for Crohn's disease that offers rapid, and sustained remission level control of symptoms and an immediate improvement in quality of life."

cA2 Marketing Plan Clinical Positioning Strategy

■ Target Audience

- Gastroenterologists
- Colorectal surgeons
- Internists (w/ high-volume IBD practice ~ 950)
- Payers

Payer Strategy Payer-Related Strategic Imperatives

- Ensure payer formulary acceptance by communicating a reasonable economic rationale for cA2 price and treatment cost
- Prevent administrative burdens from negatively impacting the cA2 prescribing decision by providing reimbursement support for physicians and patients
- Minimize constraints placed on cA2 patient selection, dosage, and treatment frequency by working with payers to implement appropriate patient access controls while minimizing patient and physician paperwork and hassle

Payer Strategy cA2 Economic Positioning Statement

■ cA2-

- a new standard of care for Crohn's disease, clearly justifies its cost to the health care system by profoundly and rapidly improving patient quality of life while offering the potential for reducing the consumption of alternate medical resources

Payer Strategy Strategic Themes

- Direct the corporate account and sales representative teams to aggressively promote the cA2 clinical platform to payers in order to secure the broadest possible coverage irrespective of the FDA-approved indication
- Rigorously prepare the field force to handle economic questions and overcome objections as they arise, but do not lead with an economic proposition
- Overcome provider "hassle-factor" by delivering premium service levels for all in-house and partner value-added programs
- Provide the field force with tools to engage in reimbursement problem solving

Payer Strategy Pre-approval

- Prepare a tactical response for all possible payer control mechanisms and scenarios
- Construct the cA2 economic platform in a way that
 - Communicates the cA2 Payer Positioning Statement
 - Leverages all of the cA2 benefits
 - Positions the cost of cA2 within the context of current treatment outcomes and costs
- Resolve the threat of a negative Medicare APG reimbursement code with lobbying efforts
- Conduct Managed Care Advisory Board meetings

Payer Strategy Post-approval, Pre-launch

- Communicate the core cA2 clinical platform to payer medical directors in order to secure formulary approval status
- If and only if payer cost concerns impede formulary approval,
 - then communicate the necessary elements of the cA2 economic platform

Payer Strategy Post-launch

- Aid providers in executing the reimbursement function and ensuring access to cA2 by deploying
 - the field force
 - a reimbursement hotline
 - an assignment of benefit partner
 - patient assistance program (indigent population)
- Establish a reimbursement surveillance function via all in-house and partner customer contact points
- For each significant control mechanism identified by the reimbursement surveillance function execute the appropriate measured tactical response

Payer Strategy Example -Measured Tactical Response

■ Control Mechanism

- Case managers reserve cA2 for patients who have failed steroids and/or immunosuppressants

■ Tactical Response Plan

- Deploy sales rep and corporate account manager to conduct case manager in-services that provide medical education on appropriate cA2 usage
- If necessary, deploy corporate account manager to review clinical platform with payer medical director in order to secure a policy change
- If unsuccessful, corporate account manager presents the economic platform
- If unsuccessful, corporate account manager pursues opinion leader and/or MCO GE support via letters, conference calls, and in-office meetings

Payer Strategy Health Economic Platform

■ Disease Overview

- The CD patient population is relatively small in comparison to other chronic medical conditions
- The moderate-severe CD patient population is a subset of all CD patients
- Moderate-severe CD patients
 - » working ill
 - » relatively young
 - » suffer from a life long miserable disease (QOL)
- Moderate-severe CD can result in
 - » disability
 - » lost productivity

Payer Strategy Health Economic Platform

■ Current Treatments

- All current treatments for moderate-severe CD have deficiencies that create an unmet patient need
 - » toxic
 - » relatively ineffective
 - » toxic and relatively ineffective
- Many CD patients require TPN or hospitalization for bowel rest
- Many CD patients require surgery; often multiple surgeries because the relapse rate is high

Payer Strategy Health Economic Platform

■ Cost Of Illness

- The cost of illness varies with severity
 - » Mild CD is fairly inexpensive to treat
 - » Moderate-severe CD is expensive to treat
- The typical moderate-severe CD patient undergoes several hospitalizations at a cost of \$25,000-\$30,000 per hospitalization
- Hospitalization and outpatient costs are driven by
 - » diagnostic
 - » medical
 - » surgical procedures
 - » physician professional fees

Payer Strategy Health Economic Platform

- The cA2 Profile
 - cA2 is effective
 - cA2 is safe
 - cA2 is a true outpatient pharmaceutical
 - Acknowledge small subset of non-responders
 - The cA2 target patient population is the moderate-severe subset of all CD patients
 - cA2 produces a profound and rapid improvement in QOL that translates into a cumulative quality of life gain in comparison to immunosuppressants

Payer Strategy Health Economic Platform

- The cA2 Economic Takeaways
 - cA2 fits within the mission of managed care (prevention, "right treatment in the right setting")
 - The cA2 appropriate patient selection schema ensures that over utilization is not an issue
 - cA2 improves health status while offering the potential for lowering costs by "converting" expensive moderate-severe patients into less costly mild patients through reduced hospitalizations and other resources

Payer Strategy Critical Success Factors

- T16 and T20 data are published in one or more compedia to serve as new-use-label proof sources
- A supplement to the ACG IBD guidelines is published and includes a favorable positioning for cA2 to serve as an new-use-label proof source
- AOB and reimbursement hotline partners provide a high level of customer service and eliminate reimbursement constraints
- BIO and PhaRMA lobbying successfully carves out expensive pharmaceuticals from the Medicare APG system

Payer Strategy Tactical Programs

- Assignment of benefit program
- Reimbursement hotline
- Patient assistance program
- Managed Care Advisory Board
- ACG-sponsored Managed Care Medical Directors conferences
- Outcomes tracking program

Payer Strategy Tactical Assets

- Publications
 - Crohn's disease economic white paper
 - T16 NEJM publication
 - T20 publication
 - Hewitt Associates cost of illness study
 - Inpatient cost studies (University of Chicago, Thomas Jefferson University Hospital, other key centers)
 - ACG guidelines supplement
- Appropriate patient selection detail kit
- Case manager in-service slide presentation
- Managed care financial impact modeling software
- Key payer dossiers
- Economic platform detail kit
- Letter of medical necessity kit
- Payer medical directors formulary kit

Integrated Services Strategy

- Addresses the following strategic imperatives
 - Establish leadership position in the treatment of IBD among gastroenterologists
 - Position cA2's IV route of administration as patient management advantage
 - Fully support in-office use of cA2 among Gastroenterologists by providing turn key services
- Goals
 - Neutralize the perceived complexity of delivering in-office cA2 infusions
 - Address physicians' concerns regarding the financial impact of in-office infusions
- Elements
 - Easy, rapid access to product and required IV administration supplies
 - Reimbursement support services
 - Guidance on clinical and administrative procedures
 - Patient education support

Integrated Services Strategy

- Product Access Needs
 - Just-in-time delivery
 - No or minimal inventory carrying costs
 - Purchase options
- Centocor will facilitate two access/purchase options
 - Assignment of Benefits
 - » Physician does not take title of drug
 - » Drug benefit is transferred to third party
 - » Third party is responsible for reimbursement clearance and payment collection
 - Direct Purchase of Product
 - » Physician takes title of product
 - » Physician receives drug benefit
 - » Physician is responsible for reimbursement clearance and payment collection

Integrated Services Strategy

■ Assignment of Benefits (AOB) Option

- Nova Factor preferred (non-exclusive) provider of AOB specialty distribution services for cA2:
 - » Prescription receipt
 - » Reimbursement pre-clearance
 - » Overnight drug and IV supplies delivery
 - » Claim adjudication
 - » Payment collection
 - » Patient counseling and follow-up
 - » Physician and patient level sales and treatment trend data collection and reporting